Analysis of brain activity involved in chewing-side preference during chewing: an fMRI study

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SUMMARY The aim of this study was to investigate the activation characteristics of cerebral cortex in participants with CSP during rhythmic chewing movement. Sixteen right-handed participants with left (two males: 29.0 ± 8.4 years old, six females: 32.3 ± 4.8 years old) or right (four males: 31.0 ± 6.1 years old, four females: 30.8 ± 4.7 years old) CSP were scanned by functional magnetic resonance imaging during rhythmic chewing. The on-off sequence of scanning was 30 s of rhythmic chewing and 30 s of rest (off) a total of five times. The results showed that blood oxygen level-dependent signals in the contralateral (to the CSP) primary sensorimotor cortex increased more than in the ipsilateral primary sensorimotor cortex in participants with both left and right CSP \((P \leq 0.001)\). Moreover, the BOLD signal within the right substantia nigra of midbrain, brainstem was more significantly \((P \leq 0.001)\) activated than its left counterpart in participants with left CSP, while no

activation was observed in those with right CSP. The similar activation of the cerebellum was in participants with right CSP. The inferior parietal lobule, inferior frontal gyrus and left insular cortex were significantly \((P \leq 0.001)\) activated in participants with CSP. These findings suggest a relationship between hemispheric dominance and CSP in the primary sensorimotor cortex responsible for rhythmic chewing movement. The brainstem and the cerebellum might also play important role in the regulation of CSP. Furthermore, the IFG, IPL and insular may contribute to higher cognitive information processing for participants with CSP.

KEYWORDS: chewing-side preference, cerebral cortex, functional magnetic resonance imaging, chewing

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Introduction

Mastication is a rhythmic function involving the coor-dinated action of peripheral effector organs, sensory input and the central nervous system. In 1985, asymmetry in masticatory behaviour in the form of chewing-side preference (CSP) was reported (1). Chewing-side preference, which is a preference for one side of the dentition where mastication is performed consistently and predominantly, is hypothesised to be an expression of motivational and/or sensorimotor behaviour influenced by peripheral factors in humans (2). It is generally accepted that the motor command for the basic pattern of rhythmical oral–facial movements is generated by a neuronal population in the brainstem central pattern generator (CPG) (3). At present, researchers disagree on whether the preferred chewing side is centrally determined or related to some peripheral factors (4, 5). It has already been demonstrated using functional magnetic resonance imaging (fMRI) that there is a relationship between CSP and hemispheric dominance in the primary sensorimotor cortex (SI/MI) responsible for bilateral tooth-clenching (6) and tongue movements (7). Little information is available regarding the activation characteristics of cerebral cortex in participants with CSP during rhythmic chewing movement. The basic patterns of mastication are known to be
controlled by a brainstem CPG. We postulate that structural and functional changes would be expected to occur in both of the SI/MI and brainstem CPG region.

In this study, we therefore used fMRI to analyse the activation characteristics of human cerebral cortex and brainstem CPG in participants with CSP, which will be helpful to explore the pathogenesis of CSP.

Materials and methods

Participants in this study were 16 patients (10 females and 6 males, aged 23–38 years) from the stomatological department at Chinese People’s Liberation Army (PLA) General Hospital. All the participants were right-handed and had full healthy dentition except for third molars. The participants were questioned about their preference for right- or left-side chewing. Also, CSP was determined by placing a piece of chewing gum (moderately hard gums without odour or taste, Nanjing, Chinese) on the centre of the dorsal aspect of the tongue and observing the direction towards which the gum was moved by the tongue for the first cycle of mastication (6, 8, 9). None of the participants had obvious changes within the bony structure of the temporomandibular joint revealed by cone-beam computed tomography, and none had pain in the temporomandibular joint during clenching. None of the participants had amalgam or metal crown restorations, which might influence image quality, and none had any history of neurological or psychiatric disorders. Using these criteria, eight participants (two males: 29-0 ± 8-4 years old, six females: 32-3 ± 4-8 years old) with left CSP and eight participants (four males: 31-0 ± 6-1 years old, four females: 30-8 ± 4-7 years old) with right CSP were chosen. They were informed in detail before the study about the nature of the experiment and were able to fully comply with the task sequence during rehearsal. All gave written informed consent to participate in this study. The study was carried out in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of Chinese PLA General Hospital.

Experimental protocol

Each participant was comfortably laid supine on the scanner table, and the head was positioned in the head-coil and immobilised with vacuum pads. All participants were instructed to minimise head movements and keep their eyes closed. Earplugs were provided to avoid auditory discomfort. They were then asked to practice rhythmic chewing tasks of moderately hard gums without odour or taste (Nanjing, Chinese) at the rhythm of 1 Hz. The task paradigm was an alternation between 30 s of rhythmic gum chewing (on) and 30 s of rest (off). This on-off procedure was repeated five times in each scanning run (Fig. 1). We cued the participant in on-off task by gently and rapidly clapping the participant’s right foot.

Image acquisition

Before each functional scan, an 8-min whole-brain, three-dimensional anatomical image-scanning procedure was performed. Functional magnetic resonance imaging was performed on a 2.0T prestige scanner*. In a single session, 20 contiguous axial slices over the entire brain (each 6 mm thick, with no gaps) were acquired using a gradient echo echo-planar (GE-EPI) T_2*-sensitive sequence [repetition time (TR) = 3000 ms, echo time (TE) = 45 ms, flip angle (FA) = 90°, matrix = 128 × 72, field of view = 373 × 212 mm]. For anatomical image scan, a high-resolution T_1-weighted structural MRI was acquired for each participant using a three-dimensional FLASH sequence (2 mm thick, no gap, TR/TE/FA = 25 ms/6 ms/28°, field of view = 220 × 220 mm, matrix = 220 × 220). Both anatomical and functional native data were transformed from the MRI into the Talairach space.

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Statistical analysis and activation determination

Image processing and statistical analysis were performed using the SPM99 software package. This statistical package was chosen because of its public availability, as well as its wide use by the neuroscience community. The first three volumes of images had to be discarded because of instability of magnetisation. All images were realigned, corrected for motion artefacts, normalised into the Montreal Neurological Institute space and smoothed using a 7-mm full width at half maximum (FWHM) Gaussian kernel. Head motion was corrected using SPM99. It was confirmed that the residual motion did not exceed 1.5 mm in translation and 0.5° in rotation in the x-, y-, and z-coordinates.

A general linear model approach was formulated by incorporation of data from all participants to describe brain activation in Brodmann’s area (BA). A t-test statistical analysis was used to determine significance on a voxel-by-voxel basis. We expressed the locations of the most significant voxels by their coordinates in the Talairach’s space, transformed from Montreal Neurological Institute coordinates. Talairach daemon client software (version 1.1†) was used for determination of blood oxygen level-dependent signals. Individual analysis was performed using the original native data sets, which generated an fMRI image of each person at a threshold level cluster volume >3 voxels and $P < 0.001$. A threshold level at cluster volume >10 voxels and $P < 0.001$ was set for group analysis to identify significant activation sites in each group.

Results

Group analysis showed (Table 1) that in the participants with left CSP, the right SI/MI was significantly $(P \leq 0.001)$ more activated than its left counterpart during rhythmic chewing (Fig. 2a). On the other hand, the left SI/MI was significantly $(P \leq 0.001)$ more activated than the right SI/MI in participants with right CSP (Fig. 2b). Moreover, the BOLD signal within the right substantia nigra of midbrain, brainstem was more significantly $(P \leq 0.001)$ activated than its left counterpart in participants with left CSP.

Table 1. Significant increases in the fMRI signal during chewing in participants with right or left CSP: anatomical regions, Brodmann’s Area (BA) and maximal t values with coordinates as given in the Talairach and Tournoux Atlas (1988)

<table>
<thead>
<tr>
<th>Participants</th>
<th>R/L Region of activation</th>
<th>BA</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Voxels</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right CSP ($n = 8$)</td>
<td>L primary sensorimotor cortex</td>
<td>3,4</td>
<td>-50</td>
<td>-2</td>
<td>17</td>
<td>226</td>
<td>13.04</td>
</tr>
<tr>
<td></td>
<td>R primary sensorimotor cortex</td>
<td>3,4</td>
<td>56</td>
<td>-2</td>
<td>19</td>
<td>-</td>
<td>21.25</td>
</tr>
<tr>
<td></td>
<td>R inferior parietal lobule</td>
<td>40</td>
<td>48</td>
<td>-25</td>
<td>32</td>
<td>254</td>
<td>23.42</td>
</tr>
<tr>
<td></td>
<td>L cingulate gyrus</td>
<td>24</td>
<td>-12</td>
<td>-7</td>
<td>45</td>
<td>68</td>
<td>13.77</td>
</tr>
<tr>
<td></td>
<td>R cingulate gyrus</td>
<td>24</td>
<td>12</td>
<td>-7</td>
<td>45</td>
<td>36</td>
<td>15.82</td>
</tr>
<tr>
<td></td>
<td>L insular</td>
<td>13</td>
<td>-36</td>
<td>3</td>
<td>11</td>
<td>80</td>
<td>12.97</td>
</tr>
<tr>
<td></td>
<td>R inferior frontal gyrus</td>
<td>47</td>
<td>48</td>
<td>15</td>
<td>2</td>
<td>93</td>
<td>8.43</td>
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<tr>
<td></td>
<td>L cerebellum</td>
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<td>-6</td>
<td>-73</td>
<td>-4</td>
<td>110</td>
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<tr>
<td></td>
<td>R cerebellum</td>
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<td>15</td>
<td>-62</td>
<td>-7</td>
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</tr>
<tr>
<td>Left CSP ($n = 8$)</td>
<td>R primary sensorimotor cortex</td>
<td>3,4</td>
<td>60</td>
<td>0</td>
<td>24</td>
<td>62</td>
<td>12.56</td>
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<tr>
<td></td>
<td>L primary sensorimotor cortex</td>
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<td>-56</td>
<td>-2</td>
<td>25</td>
<td>-</td>
<td>16.65</td>
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<tr>
<td></td>
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<td>50</td>
<td>37</td>
<td>-12</td>
<td>373</td>
<td>25.30</td>
</tr>
<tr>
<td></td>
<td>L insular</td>
<td>13</td>
<td>-36</td>
<td>6</td>
<td>8</td>
<td>339</td>
<td>18.42</td>
</tr>
<tr>
<td></td>
<td>L putamen, basal ganglia</td>
<td>-</td>
<td>-15</td>
<td>3</td>
<td>0</td>
<td>42</td>
<td>13.24</td>
</tr>
<tr>
<td></td>
<td>R brainstem, midbrain</td>
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<td>-15</td>
<td>-9</td>
<td>28</td>
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<tr>
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<td>-</td>
<td>-9</td>
<td>-12</td>
<td>-7</td>
<td>-</td>
<td>9.01</td>
</tr>
</tbody>
</table>

R, right; L, left; CSP, chewing-side preference.

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However, there was no activation of substantia nigra of midbrain, brainstem activated in participants with right CSP (Fig. 3b). In addition, the BOLD signal within the left cerebellum was more significantly ($P \leq 0.001$) activated than right cerebellum in participants with right CSP (Fig. 3b). However, there was no activation of cerebellum in participants with left CSP (Fig. 3a).

Among the activated regions, the inferior parietal lobule (IPL) ($z = 36$) and inferior frontal gyrus (IFG) ($z = 0$) were significantly ($P \leq 0.001$) activated in participants with right CSP (Fig. 4a). The right IFG ($z = -12$) in patients with left CSP was significantly ($P \leq 0.001$) activated (Fig. 4b). Furthermore, the significant activation of left insular cortex was found in participants with both right (Fig. 4a) and left (Fig. 4b) CSP.

**Discussion**

Some studies using fMRI have demonstrated that chewing or mandibular movement significantly activates the SI/MI in healthy volunteers (12, 13). Moreover, there appear to be no significant differences between the right and left hemispheres during rhythmic chewing (12, 14). In this study, blood oxygen level-dependent signals within the contralateral SI/MI were significantly more activated than the ipsilateral SI/MI in participants with both left and right CSP. Our results suggest a relationship between contralateral hemispheric dominance and CSP in the areas of the SI/MI responsible for rhythmic chewing tasks, which is consistent with our previous findings for tooth-clenching movements (6) and other findings for tongue movements in participants with CSP (7). Moreover, the interesting results in this study were bilateral substantia nigra of midbrain, brainstem activated in participants with left CSP, and the BOLD signal within the right substantia nigra of midbrain was more activated than its left counterpart. The similar result of the cerebellum was in participants with right CSP. The results indicate that substantia nigra of midbrain and the cerebellum may participate in the regulation of rhythmic chewing in participants with CSP. However, there were no brainstem activated in the group analysis results of participants with right CSP and no cerebellum activated in participants with left CSP, although there was left brainstem activated in one participant with right CSP in the individual-based analysis of the present study.

It is well known that the fundamental pattern of mastication — rhythmic opening and closing of the...
jaws – and the associated repetitive movements of the tongue, cheeks and lips can be generated by a brainstem central pattern generator (CPG) in the absence of sensory feedback. The intrinsic pattern of mastication is generated by CPG located in the pons and medulla. It is impossible to carry-out mastication using only the muscles on one side of the mandible, but Nozaki et al. (15, 16) showed that if the two sides of the caudal pons and medulla are separated, each side of the brainstem is able to generate a unilateral pattern. The output of the CPG is modified by inputs that descend from higher centres of the brain and by feedback from sensory receptors. It has also been shown that an increase in the masticatory force elevates activities in the masseter muscle, where sensory information is finally projected to the cerebellum (17). Iida et al. suggested that the influence of periodontal afferent inputs and associated jaw muscle activity on cerebral activity was relatively minor compared to the rhythmic jaw movements. It suggest that cerebral activity during rhythmic jaw movements is not influenced by the phasic inputs from periodontal mechanoreceptors, but rather is reflecting the continuous and rhythmic activity from muscle spindles, and other mechanoreceptors related to jaw movement (18). We presume that contralateral hemispheric dominance of the SI/MI in participants with CSP, the cerebellum in participants with right CSP and the substantia nigra of midbrain, brainstem in participants with left CSP are probably related to subconscious and preferred rhythmic chewing movement (19). However, the differences between the participants with left and right CSP need further study.

In consistent with our previous finding that the IFG and IPL were coactivated during clenching in participants with both right and left CSP (6). In this study, we also found that the IFG and IPL were coactivated in participants with right CSP and IFG was activated in participants with left CSP during rhythmic chewing. The IFG, a neocortical area in the frontal lobe, is involved in integrating various stimuli and planning appropriate behaviours. After studying rabbits with IFG lesions, McLaughlin and Powell suggested that this area was involved in retrieval of information that determined performance of the jaw movement response (20). The IFG, in classically also known as Broca’s area, has been shown to be involved in skill acquisition. It is known that the inferior parietal lobule (IPL) was associated with the manipulating process. It is also reported that electrical stimulation of IPL generates an endogenous and unspecific experience of ‘wanting to act’ (21). Parietal neurons encode spatial information, but they also encode non-spatial, executive and motivational aspects of complex tasks. Also, the role of the IPL during initial motor learning can be attributed to the integration of sensory information and feedback processing (22). Thus, combining the findings in the...
present study and these observations, it could be thought that the IFG and IPL are involved in higher cognitive information processing during rhythmic chewing task to control the pattern and frequency of chewing according to a precise feedback control.

The insula has been considered a supplementary motor region or a motor association area, respectively. Recent research implicates the insula in a wide variety of cognitive, sensory and emotional functions. It is also reported that this region constituted a crucial part of the executive networks (19). It has been demonstrated that chewing resulted in a bilateral increase in the BOLD signals in the sensorimotor cortex, cerebellum, thalamus, supplementary motor area and insula. There appear to be no significant differences between the right and left hemispheres (23). However, in the present study, we found the significant activation of left insular cortex in participants with both left and right CSP, which might reflect the insular laterisation in regulation the rhythmic chewing in participants with CSP.

Evidence from electrophysiological studies and hemispheric inactivation procedures has indicated strong lateralisation of affective processing within the insula based on autonomic input to this region. However, inconsistent results have come from lesion studies in patients and findings from functional neuroimaging studies (24). A recent investigation reported a link between structural insula asymmetry and functional language lateralisation and found that the anterior insula asymmetry was associated with lateralised word recognition. Then, the role of left insular on the chewing-side preference need further study.

In conclusion, a relationship exists between hemispheric dominance and CSP in the SI/MI responsible for the rhythmic chewing task. The brainstem and the cerebellum might also play important role in the regulation of CSP. Furthermore, the IFG, IPL and insular may contribute to higher cognitive information processing for participants with CSP. However, an increase in sample size would help to confirm the findings.

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References


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